TB CASE INVESTIGATION AND CASE MANAGEMENT PARTNERSHIP IN CARE

Division of Global Populations and Infectious Disease Prevention
Bureau of Infectious Disease and Laboratory Sciences
Massachusetts Department of Public Health
Welcome

Effective TB response requires knowledge, skills, and partnerships – and comes with challenges and opportunities.

New introductory/foundational training series for:
- New local public health partners
- Local public health nurses who haven’t provided TB case management recently

Hope to illustrate shared partnerships essential to disease response.
Series of three webinars

- Introduction to Tuberculosis (today)
- Introduction to TB Disease Response (June 17)
- Introduction to TB Contact Investigations (July 1)

Participation in all webinars is not required - if you miss the any webinar you can still attend the others.
INTRODUCTION TO TUBERCULOSIS

John Bernardo, MD
TB Medical Officer, DPH
Professor of Medicine, Boston University School of Medicine
Session One Objectives

- Provide Basic Overview of Tuberculosis
- Discuss Clinical presentation of suspected tuberculosis
- Identify Diagnostic tests to rule out tuberculosis
- Discuss treatment options for persons with suspected active tuberculosis

Conflicts, John Bernardo, MD: None
Tuberculosis

- TB is an Infectious Disease
  - Endemic in the world today
  - Reservoir of infected persons
- The disease can involve any organ/system
  - Respiratory system (lungs/airways) most common form
- Can be spread from person to person (*airborne*)
  - *Not* very contagious
- May be difficult to diagnose
  - *Suspicion* is most important
- Is treatable
  - Treatment cures the disease
- *Is preventable*
  - Reduces reservoir of infected persons
How is TB Transmitted?

- Airborne transmission by aerosolization
- Coughing
- Laughing
- Singing
- Sneezing

- Needs prolonged exposure to infected air
How TB is NOT transmitted

- Casual contact
- Through food
- Shaking hands
- Short exposure time
Disease Transmission

- TB is spread through the air
- Once inhaled, bacteria travel to lung alveoli and establish infection
- Organisms carried by circulatory and lymphatic systems
- 2–10 wks after infection, developing immune response limits activity; infection is detectable by testing for immune response to TB proteins (TST or IGRA)
  - Immune system contains (“walls off”) bacteria in granulomas
  - Some bacteria survive and remain viable for years as they try to overcome immune containment to replicate and cause TB disease

MOST TB today represents “reactivation” of LTBI
Other possible sites of disease

Main sites of Extrapulmonary tuberculosis

- Central nervous system
  - Meningitis

- Lymphatics
  - Scrofula (of the neck)

- Pleura
  - Tuberculosis pleurisy

- Disseminated
  - Miliary tuberculosis

- Bones and joints of spine
  - Pott's disease

- Genitourinary
  - Urogenital tuberculosis
TB Infection to TB Disease

TB infection

- Recently infected
- Underweight
- Diabetes
- HIV/AIDS

TB disease

- Very young/old
- Certain Cancers

Without any additional risk factors, 1 in 5-10 people who are infected with TB will become sick with TB disease in their lifetimes.

Most (>75%) TB in the US today results from activation of LTBI.
The Tuberculosis Continuum

**TB Infection (LTBI)**
- TB bacteria in organ but contained
- TST or blood tests usually positive
- No symptoms
- Chest X-ray is usually normal
- Negative bacteriology
- Not infectious
- Multiple treatment options

**Active Disease**
- TB bacteria in organs or tissues but multiplying
- TST or blood tests usually positive
- Symptomatic
- Positive bacteriology
- Abnormal diagnostic tests, chest X-ray, CT scans
- Infectious if pulmonary
- Standard treatment 6 months
Determining TB Risk

- Birth or residence in a country with higher rate of TB (any country other than the US, Canada, Australia, New Zealand, or Western/Northern Europe)
- Immunosuppression - History of immuno-suppressive disease or taking medications that could cause immuno-suppression
- Co-morbid condition(s) that may increase risk including end stage renal disease, diabetes mellitus, malignancy
- Close contact to someone with infectious tuberculosis
Diagnosing TB Infection: Interferon Gamma Release Assays (IGRAs)

- Blood test for TB infection
  - Results reported as positive, negative, indeterminate and/or borderline
- Performed on children ages 2 and older
- Does not cross-react with BCG
- Not recommended for serial testing
- Approved products include QuantiFERON® - TB Gold Plus, and T-Spot® - TB
IGRAs

- Whole-blood tests used to detect TB infection
- T Cell-based technologies
  - Measure immune sensitization/response to TB proteins
- Blood incubated 16-24 hours with
  - TB-specific antigens ESAT-6 and CFP-10
  - Mitogen
  - Buffer (control)
- Cells that recognize antigen release interferon-γ
- [Interferon] released in response to TB antigens compared to amount released in response to non-antigenic stimulus (mitogen)
Diagnosing TB Infection – Tuberculin Skin Test

Tuberculosis Skin Test (TST)

- Intra-dermal planting and read 48 – 72 hours later
- Tuberculin solution (Purified Protein Derivative – PPD)

Standardized:
Tuberculin Skin Test

Skin test interpretation depends on
- The measurement in millimeters of the induration (NOT erythema) **across** the forearm
## Interpretation of PPD

**Depends on the patient risk**

<table>
<thead>
<tr>
<th>Size of PPD</th>
<th>Who should be considered positive?</th>
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<tbody>
<tr>
<td>≥ 5 mm</td>
<td>1. Immunosuppressed person, especially HIV+&lt;br&gt;2. Close contact of infectious TB case&lt;br&gt;3. Lesion on CXR consistent with old TB</td>
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<tr>
<td>≥ 10 mm</td>
<td>1. From a high incidence group (<em>e.g.</em>, from area where TB is endemic such as certain foreign countries, prisons, nursing homes, homeless shelters; intravenous drug user)&lt;br&gt;2. Recent PPD converter (2 yr; &gt;10mm)</td>
</tr>
<tr>
<td>≥ 15 mm</td>
<td>1. No known risk factors for TB</td>
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Factors affecting TST results

False positives
- Non-tuberculosis mycobacterial infections
- Bacillus Calmette-Guérin (BCG) vaccination
- Prior treatment of bladder cancer with BCG
- Use of Aplisol®

False negatives
- Recent Infection
- Young age (<6 months old)
- Anergy
- TB Disease
- Recent live virus vaccine
- HIV infection
- Other immuno-suppression
BCG Vaccination

- BCG: Live attenuated strain of *Mycobacterium bovis*.
  - Developed by Calmette and Guérin for use as vaccine - first administered to humans in 1921.
- The only vaccine against tuberculosis in general use.
- BCG is the most widely administered vaccine in the world.
- Limited prevention activity.
  - TB meningitis in children in high prevalence countries.
- In the US, BCG was never adopted for routine childhood immunization.

* Bacille Calmette Guérin
Is it tuberculosis?

Clinical presentation with diagnostic testing and social information is factored into initial diagnostic process. This usually is

*Clinical – based on Suspicion*

*Confirmed – may take time*
Diagnosis of TB – Putting Together a Clinical Picture

- Symptoms
- Epidemiology*
  - Where is the person from?
    - >80% MA cases are non-US born
  - Recent travel history
  - Is he/she a contact to a known case?
- TB infected?
  - TST or IGRA positive
- Diagnostic testing
Symptoms of TB Disease

- Prolonged cough
- Coughing up blood
- Fever, chills
- Night sweats
- Fatigue
- Loss of appetite
- Weight loss
- Depends on part of body affected
- Cases of suspected TB are reportable to MDPH
Diagnostic Testing

Radiology

PA CXR – single view (adults)

CT chest

Laboratory

Smear – nonspecific but available within 24hr

Culture – specific, 1-8 weeks

*Positive TST or IGRA only SUPPORTS diagnosis, may be neg in 20% of culture + TB*
TB Diagnostics Labs

GeneXpert® ("PCR")

Other laboratory tests

- Identification
  - Probe or MALDI-TOF
- Drug susceptibility testing
  - Culture-based or Molecular Detection of Drug Resistance (MDDDR)
- Genotyping

Respiratory specimens (sputum) only; results usually available within hours
INITIATION (Intensive) PHASE
Four drugs “RIPE” to start:

- Rifampin (RIF)
- Isoniazid (INH)
- Pyrazinamide (PZA)
- Ethambutol (EMB)
- +/- Vitamin B6

Duration: 2 months, will depend on drug susceptibility, patient’s tolerance
Treatment for Tuberculosis Disease

CONTINUATION PHASE
Two drugs:
- Isoniazid
- Rifampin
- +/- Vitamin B6

Continuation phase will be 4 months or more depending on patient’s tolerance, clinical presentation, extent and site of disease, and 8-week sputum culture conversion.
TB Treatment

- May also be influenced by known drug resistance of index case if the individual is a contact to a known case
- The phases of TB treatment will vary depending on initial therapy and response to therapy
- Treatment can cause side effects and close monitoring by providers and local case managers is required
- Medications can be in pill, liquid, or parenteral form
- Give medications 1 month at a time to facilitate monitoring/safety
Response to Therapy

Monitor treatment at least MONTHLY
Adherence, tolerance, safety, clinical response

How do we gauge clinical improvement?

- Improvement of TB symptoms
- Decreasing numbers of organisms seen on serial sputum smears
- Culture conversion to negative by end of initial phase; if not, extend treatment
- Improvement in CXR or other diagnostic tests

Treatment completion is based on number of doses ingested consistently over a given time period
Take Home Points

- Tuberculosis is a potentially infectious bacterial disease
- Tuberculosis can affect any organ in the body
  - Symptoms will reflect organ involvement
- One quarter of the world’s population is infected with TB
  - Tuberculosis infection usually remains contained by the immune system (termed Latent TB Infection; LTBI)
  - Most TB in the US occurs from “activation” of latent infection
  - Latent infection can be treated with 1 or more drugs to prevent future disease
- Persons with infectious tuberculosis can spread the disease to others especially when in the respiratory tract
  - Treatment can be 6 months or more with multiple antibiotics
MDPH resources

- Technical Assistance – Just-in-time training, nursing, medical consultation
- Contact investigation support with PPD or IGRA testing
- Community Health Worker support
- Transportation services
- Strategic thinking re options for contact investigation and case management
- Available through course of treatment - from early diagnosis to completion of therapy
General Resources

- Local Public Health Institute – Infectious Disease Case Management  [https://sites.bu.edu/masslocalinstitute/2014/06/23/disease-case-management/](https://sites.bu.edu/masslocalinstitute/2014/06/23/disease-case-management/)
- MDPH TB Program  [www.mass.gov/tuberculosis](http://www.mass.gov/tuberculosis)
Thank you